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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/648,759	08/25/2003	Kevin J. Brodbeck	ARC 2882 N1 (3139-6225.1U	3721

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TRASK BRITT
P.O. BOX 2550
SALT LAKE CITY, UT 84110

EXAMINER	
BARNHART, LORA ELIZABETH	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
12/13/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTOMail@traskbritt.com

Office Action Summary	Application No.	Applicant(s)	
	10/648,759	BRODBECK ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-35* is/are pending in the application.

4a) Of the above claim(s) *15 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-14,16-28 and 30-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 September 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments

Applicant's amendments filed 9/14/07 to claims 1, 5, and 9 have been entered. Claim 3 has been cancelled. No claims have been added. Claims 1, 2, and 4-35 remain pending in the current application, of which claims 1, 2, 4-14, 16-28, and 30-35 are being considered on their merits. Claims 15 and 29 remain withdrawn from consideration at this time. Prior art references not included with this Office action can be found in a prior action.

Applicant's attention is drawn to 37 C.F.R. 1.121(c) (1), which reads, "The claim listing shall commence on a separate sheet of the amendment document and the sheet(s) that contain the text of any part of the claims shall not contain any other part of the amendment." In other words, no text other than the claims themselves should appear in the claim listing; this includes introductory paragraphs such as that at the top of page 5 of the reply. Failure to comply with this rule in the future will result in the mailing of a notice of non-compliant claim amendment.

Applicant's elections without traverse of the species "human growth hormone," "benzyl benzoate," and "C_{16}-C_{24} fatty acid esters" are still in effect over the claims.

Priority

The examiner thanks the applicant for clarifying the priority of the cited applications and those to which benefit is claimed.

Specification

The objection to the specification is withdrawn.

Drawings

The drawings were received on 9/14/07. These drawings are acceptable.

Claim Objections

The claim objection of record is withdrawn.

Claim 25 is objected to because of the following informalities: A comma has been omitted between "cDNA" and "proteins" at line 2. Correction is required.

Claim Rejections - 35 USC § 102

The rejection of record over 35 U.S.C. § 102 is withdrawn in light of the claim amendments incorporating the limitations of now-canceled claim 3 into claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4-14, 16-28, and 30-35 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Brodbeck et al. (2000, U.S. Patent 6,130,200; 5/25/05 IDS) taken in view of Yamagata et al. (1997, U.S. Patent 5,628,993; 5/25/05 IDS) and Ayer et

al. (2000, U.S. Patent 6,096,339). Brodbeck is prior art under 35 U.S.C. § 102(e) because the application was filed in the U.S. before the current application and the inventive entity differs from that of the instant application; see M.P.E.P. § 2136.04.

Brodbeck teaches a sustained-release pharmaceutical composition comprising particles of spray-dried, lyophilized human growth hormone (HGH, an active agent that is a water-soluble polypeptide) and zinc acetate (a solubility modulator) suspended in a gel of poly-(D,L-lactide-co-glycolide) (PLGA, a biocompatible gel carrier) and benzyl benzoate (a solvent) (Example 2; column 23, line 45, through column 26, line 16). Brodbeck teaches that the solubility modulator, *i.e.*, an agent that alters the solubility of the active agent with reference to the polymer solvent or water (column 10, lines 17-29), may be a lipid or oil (column 15, lines 39-43, especially line 42). Brodbeck teaches making this composition by mixing a biocompatible polymer with the benzoic acid solvent to form a viscous gel, dispersing an active agent associated with a solubility modulator into the gel, and adding further components as desired (column 6, line 62, through column 7, line 7); specifically, Brodbeck teaches spray-drying a mixture of HGH and zinc acetate to yield 2-100 micron particles (column 23, line 50, through column 24, line 27).

Brodbeck does not exemplify a composition in which the solubility modulator is hydrophobic, specifically a fatty acid ester, more specifically a C_{16}-C_{24} fatty acid ester, more specifically a mixture of stearic acid and palmitic acid in particular proportions. Brodbeck does not teach making the particles comprising the active agent by crushing a compressed mass of active agent.

Yamagata teaches a sustained-release pharmaceutical composition comprising powdered particles comprising interferon-α (a water-soluble polypeptide) dispersed in a matrix of tetraglycerol dipalmitate (a fatty acid ester of palmitic acid) or tetraglycerol distearate (a fatty acid ester of stearic acid) (Examples 1-3; column 8, lines 3-37; column 6, lines 21-38). The composition of Yamagata may comprise hormones (column 4, lines 25-32). Yamagata teaches that the composition may comprise more than one fatty acid diester (column 5, lines 32-34; column 6, lines 4-5) and that the amount of each fatty acid diester in the composition may be optimized (column 6, lines 39-45).

Ayer teaches that particles comprising active agents that are included in controlled-release pharmaceutical compositions may be made by spray-drying or crushing, among other methods (column 13, lines 15-21).

A person of ordinary skill in the art would have had a reasonable expectation of success in substituting the palmitic acid and stearic acid diesters of Yamagata for the zinc acetate as a solubility modulator in the composition of Brodbeck because Brodbeck suggests that lipids and oils may act as solubility modulators. The skilled artisan would have been motivated to substitute the diesters of Yamagata for the zinc acetate in the composition of Brodbeck because Yamagata teaches that the diesters protect physiologically active peptides from hydrolysis and preserve their activity, allowing for sustained release of active polypeptide (column 2, lines 14-19).

The selection of the amount of palmitic acid diester and stearic acid diester to include in the composition of Brodbeck would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that Yamagata

teaches that the amount of a given diester in a sustained-release composition is widely optimizable (column 6, lines 39-45). A holding of obviousness over the cited claims is therefore clearly required.

The selection of the method used to make particles comprising HGH and the solubility modulator in the method of Brodbeck would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that Ayer teaches that spray-drying and crushing are art-accepted equivalents for yielding particles of dried pharmaceuticals, including polypeptides (column 11, lines 37-47, especially line 41). A holding of obviousness over the cited claims is therefore clearly required.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to substitute various amounts of palmitic acid diester and stearic acid diester for the zinc acetate in the composition of Brodbeck and to substitute crushing for spray-drying in the method of procuction because Yamagata teaches that fatty acid diesters are solubility modulators, because Brodbeck suggests that the solubility modulator may be a lipid, and because Ayer establishes the art-recognized equivalence of crushing and spray-drying for producing particles of pharmaceutically active agents.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Applicant alleges that Brodbeck does not teach a composition comprising a compressed mixture as instantly claimed (Reply, page 13, last paragraph, through page

14, last paragraph). Applicant urges that the secondary references do not remedy the alleged defects of Brodbeck (Reply, page 15, first paragraph). These arguments have been fully considered, but they are not persuasive.

First, as a matter of formality, applicant is requested to refer to pages and line numbers in the as-filed application, not to paragraph numbers in the published application. The specification being considered is that filed by applicant.

Applicant alleges that the term "compressed" means "having been subjected to compression, i.e. put under high pressure (Reply, page 14, first paragraph). However, this definition differs from the explicit definition of this term in the as-filed specification. At page 12, lines 26-28, the specification defines "compressed" as "compressed or compacted such that its bulk density after compression or compaction is greater than it was prior to compression or compaction." All that is required by this definition is that a compressed composition has greater density than the same composition when it has not been compressed. Brodbeck teaches spraying a 5 mg/mL aqueous solution of human growth hormone (HGH) onto a solid surface, then allowing it to dry into solid particles (see column 23, line 50, through column 24, line 27). These particles yielded by the drying method of Brodbeck are "compressed" since the water has evaporated from the composition prior to the drying, yielding a composition whose bulk density is greater than it was prior to the drying. Applicant is advocating a product-by-process-type interpretation of the claim term "compressed," which is improper since the term is explicitly defined at page 12 simply in terms of the relative density of a composition.

The secondary references were cited for their teachings of alternative solubility modulators (Yamagata) and methods of making pharmaceutical compositions (Ayer).

No claims are allowed. No claims are free of the art.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

IRENE MARX
PRIMARY EXAMINER

Lora E Barnhart

/lb/